UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

FEDERAL TRADE COMMISSION and

THE PEOPLE OF THE STATE OF NEW YORK, by LETITIA JAMES, Attorney General of the State of New York,

Plaintiffs,

v.

QUINCY BIOSCIENCE HOLDING COMPANY, INC., a corporation;

QUINCY BIOSCIENCE, LLC, a limited liability company;

PREVAGEN, INC., a corporation d/b/a/ SUGAR RIVER SUPPLEMENTS;

QUINCY BIOSCIENCE MANUFACTURING, LLC, a limited liability company; and

MARK UNDERWOOD, individually and as an officer of QUINCY BIOSCIENCE HOLDING COMPANY, INC., QUINCY BIOSCIENCE, LLC, and PREVAGEN, INC.,

Defendants.

Case No. 1:17-cv-00124-LLS

REPLY MEMORANDUM OF LAW IN FURTHER SUPPORT OF DEFENDANTS' MOTION TO EXCLUDE PLAINTIFFS' EXPERTS

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Defendants Quincy Bioscience Holding Company, Inc., Quincy Bioscience, LLC, Prevagen, Inc., Quincy Bioscience Manufacturing, LLC, and Mark Underwood (collectively, "Quincy" or "Defendants") respectfully submit this reply memorandum of law in further support of Defendants' Motion to Exclude Plaintiffs' Experts, filed on September 1, 2022 (Dkt. 307) ("Motion" or "Mot.") and in response to Plaintiffs' Opposition filed on October 3, 2022 (Dkt. 313) ("Opposition" or "Opp.").

PRELIMINARY STATEMENT

Quincy's Motion established that the testimony of each of Plaintiffs' four experts—Drs. Mary Sano, Janet Wittes, Jeremy Berg, and Peter Malaspina—should be excluded because they are of no help to the trier of fact on the dispositive issue in this action: whether Quincy possesses "competent and reliable scientific evidence" under the standard articulated in the FTC Guidance. Plaintiffs' Opposition does nothing to contradict the fact that each of Plaintiffs' experts' opinions are irrelevant and unreliable.

Drs. Sano and Wittes. Neither Dr. Sano nor Dr. Wittes considered the appropriate substantiation standard for dietary supplement marketing claims. Rather, they created and applied their own heightened substantiation standard—a standard that is at odds with the FTC Guidance itself and is aligned with what the FDA requires for new drug applications. Plaintiffs admit that Drs. Sano and Wittes did not review the FTC Guidance at all and make the outrageous argument that their experts had "no reason to look" at it. But expert witnesses do not offer opinions in a vacuum and must consider the relevant legal standards in order to offer opinions that "fit" the case. Because Drs. Sano and Wittes failed to consider the FTC Guidance, their opinions are irrelevant and should be excluded.

Worse still, Dr. Sano's and Dr. Wittes' criticisms of Quincy's double-blind, randomized, placebo-controlled clinical trial—the Madison Memory Study—are all based on unfounded

speculation that is contradicted by the evidence in the record. Plaintiffs pled in their Complaint that the data analysis from the AD8 0-1 and 0-2 groups was "*post hoc*" and somehow unreliable. There is simply no evidence to support Plaintiffs' allegations. Drs. Sano and Wittes' *assumed* that there was and ignored undisputed evidence to the contrary. But even if the analyses *were post hoc*, there is nothing unreliable about analyses that are not "pre-specified" in a study protocol as Plaintiffs would require. It is well-established that such purely speculative expert opinions should be excluded.

Dr. Berg. Plaintiffs' Opposition entirely ignores Dr. Berg's lack of qualifications to opine on Prevagen®'s efficacy. Although Dr. Berg claims to have been retained to consider whether there are any plausible mechanisms of action for Prevagen, his penultimate conclusion is that "it is *clear* that Prevagen and its active ingredient apoaequorin have not been shown to have *any* therapeutic effect on humans." But Dr. Berg, a chemist, admittedly does not possess expertise in memory, cognition, and/or digestion to draw such a broad conclusion. Further, Dr. Berg's opinion is grounded in the incorrect premise that there must be an established mechanism of action for Prevagen for it to have a beneficial effect. But there is no such requirement—in the FTC Guidance or any law or regulation—that there must be an established mechanism of action for dietary supplements. Such a stringent standard is not even required for drugs. Dr. Berg (who also failed to review the FTC Guidance) assumes otherwise. Finally, Dr. Berg's opinion is unreliable because he failed to consider all plausible mechanisms of action for Prevagen. While he considered *certain* mechanisms that Quincy had previously suggested were possible, his analysis was by no means comprehensive, and he did no investigation of his own whatsoever to determine whether any other mechanisms were plausible. He also summarily discounted a mechanism of action that a number of Quincy's experts found to be plausible—the gut brain axis—despite having no personal

experience with such a theory other than attending a few seminars and testifying that it is a promising and developing area of scientific inquiry. Dr. Berg's opinions are therefore irrelevant, unreliable, and would cause the jury to be confused. They should be excluded.

Dr. Malaspina. Plaintiffs' Opposition confirms that the testimony of their rebuttal expert—Dr. Peter Malaspina—should be excluded because he is an alleged expert in economics and statistics, but is offering an opinion on a specific computer programming function that he has no recollection of using until this litigation. And he is unqualified to do so. Further, the "correction" that Dr. Malaspina purportedly ran against the SUR analysis conducted by Dr. Beales is not a "correction" at all. Rather, he performed a different type of analysis using different computer language, and admitted he could not replicate the SUR analysis performed by Dr. Beales. He should not be permitted to testify about Dr. Beales' SUR, which he could not replicate, nor should he be permitted to testify about his "new" analysis, which was not run or utilized by any of Quincy's experts. Dr. Malaspina's testimony would do nothing more than confuse the jury.

ARGUMENT

I. THE OPINIONS OF DR. SANO AND DR. WITTES SHOULD BE EXCLUDED

A. The Opinions of Dr. Sano and Dr. Wittes Are Irrelevant Because They Applied the Wrong Standard

In its opening brief, Quincy explained that Dr. Sano's and Dr. Wittes' opinions are irrelevant: they offered opinions about whether Quincy's scientific substantiation evidence amounted to "competent and reliable scientific evidence" without considering the FTC's own definition of that term. (Mot. at 7-16.) Drs. Sano and Wittes instead viewed that scientific evidence against their own subjective standard—one that they admitted is the same heightened standard that would be applied to a drug trial—in place of the appropriate standard for dietary

supplements set out in the FTC Guidance. Plaintiffs' argument in their Opposition does nothing to change that.

Plaintiffs acknowledge that the central question in this case is whether Quincy's marketing claims are substantiated by "competent and reliable scientific evidence." They also acknowledge that the FTC Guidance contains the applicable definition of that term. (Opp. at 9.) But Plaintiffs then go on to argue that—somehow—Drs. Sano and Wittes had "no reason or need to look" at the FTC Guidance (perhaps, because it is diametrically opposed to their heightened standard). (Opp. at 10.) The disconnect in that position jumps off the page. Plaintiffs agree that the FTC Guidance sets out the applicable standard for what counts as "competent and reliable scientific evidence," but their expert witnesses were permitted to ignore the FTC Guidance and create their own standard to determine what constitutes "competent and reliable scientific evidence." That makes no sense and Plaintiffs' Opposition makes no attempt to reconcile the free pass they grant their experts on this critical issue. A simple example (from the Advisory Committee Notes to the Federal Rules of Evidence) illustrates just how absurd Plaintiffs' position is. An expert surely cannot, for example, offer an opinion about an individual's capacity to make a will without knowing the legal elements of testamentary capacity and analyzing those elements. *See* Fed. R. Evid. 704 (Advisory Committee Notes) (stating that an opinion on whether "'[testator had] sufficient mental capacity to know the nature and extent of his property and the natural objects of his bounty and to formulate a rational scheme of distribution' would be allowed"). Experts do not offer opinions in a vacuum. To be admissible, their opinions must "fit" the case. *See Malletier v. Dooney & Bourke, Inc*., 525 F. Supp. 2d 558, 662-63 (S.D.N.Y. 2007). As set forth in Quincy's opening brief, Dr. Sano's and Dr. Wittes' opinions do not fit this case.

Plaintiffs' analytical leaps grow larger. Plaintiffs next suggest that Drs. Sano and Wittes *actually did* apply the standard articulated in the FTC Guidance—despite admitting that they did not know it existed, look at it or know what it said. (*See e.g.*, Dkt. 259-11, Wittes Tr. at 37:17-18 ("I have no idea where the phrase [competent and reliable scientific evidence] comes from with respect to dietary supplements.").) Plaintiffs baldly suggest Dr. Sano's and Dr. Wittes' analyses were "entirely consistent" with the FTC Guidance's definition of "competent and reliable scientific evidence." (Opp. at 10.) But Plaintiffs do not point to any sections of their reports or any portions of their deposition testimony to demonstrate any such consistency. (*Id.*) Nor do they spell out how Drs. Sano and Wittes engaged with and applied a substantiation standard that they did not know existed. (*Id.*) Rather, Plaintiffs simply conclude there is "no 'analytical gap' between the language of the FTC Guidance and the analyses performed by Drs. Sano and Wittes," based on Plaintiffs' own say so and nothing more. (*Id*.)

To start, Drs. Sano and Wittes admittedly applied a heightened standard that mirrors the FDA's standard for the approval of new drugs. At their depositions, both Dr. Sano and Dr. Wittes explained that, in their view, the substantiation standards for drugs and dietary supplements are the same. (Dkt. 259-10, Sano Tr. at 49:16-22; Dkt. 259-11, Wittes Tr. at 26:21—27:2.) That approach is profoundly inconsistent with the FTC Guidance. The FTC Guidance was issued in response to the Dietary Supplement Health and Education Act of 1994 ("DSHEA"). *See U.S. v. Bayer Corp*., No. 2:07-cv-00001, 2015 WL 5822595, at *3 (D.N.J. Sept. 24, 2015) (because "DSHEA does not specify what substantiation is necessary to render a claim 'truthful and not misleading,'" the FTC "provided guidance, stating that the relevant standard is 'competent and reliable scientific evidence'"). And DSHEA made clear that the law treats dietary supplements and drugs differently, subjecting them to different substantiation standards. *See id.*; *see also* S.

784, 103rd Cong. § 2(b)(2)(B) (1994) ("It is the purpose of [the DSHEA] to . . . clarify that . . . dietary supplements should not be regulated as drugs."). This distinction is embodied in the FTC Guidance: "Where there is an existing standard for substantiation developed by a government agency or other authoritative body, the FTC accords great deference to that standard." (Dkt. 308-1 at 9 ("FTC Guidance").) Without even knowing of the existence of the FTC Guidance, however, Drs. Sano and Wittes believed otherwise. Perhaps this is because they have no expertise in dietary supplement claim substantiation. (Dkt. 259-10, Sano Tr. at 67:11-13, 74:9-12; Dkt. 259-11, Wittes Tr. at 37:19—38:22.) Their basic misunderstanding of the substantiation standard that applies to dietary supplements—standing alone—underscores the disconnect between their own heightened standard and the applicable standard in the FTC Guidance.[1]

Worse still, Dr. Sano directly contradicted the FTC Guidance. According to Dr. Sano, "[t]esting on humans is necessary" and "competent and reliable scientific evidence" can *only* take the form of "at least one randomized, well-controlled, double-blind clinical trial." (Dkt. 308-2, Sano Report ¶¶ 28-29.) But that is the *opposite* of what the FTC Guidance says. ("The FTC will consider *all forms* of competent and reliable scientific research when evaluating substantiation.") (FTC Guidance at 10.) Although randomized placebo-controlled human clinical trials are unquestionably a reliable form of evidence (Quincy's own experts do not argue otherwise), they are not the *only* form of reliable scientific evidence and the FTC Guidance does not—in any way—limit the analysis to only human clinical trials. In fact, the FTC Guidance specifically advises that "[t]here is no fixed formula for the number *or* type of studies required" and expressly mandates

[1] Indeed, the simple fact of Plaintiffs' retention of Drs. Sano and Wittes—whose experience lies almost exclusively in the pharmaceutical context—is contrary to the FTC Guidance. Indeed, the FTC Guidance provides that in making a determination of "competent and reliable" scientific evidence, "the FTC consults with experts from a wide variety of disciplines, including those with experience in botanicals and traditional medicines." (FTC Guidance at 9.) Plaintiffs' retention of experts who lack experience with dietary supplements further confirms that those experts' opinions do not "fit" the case.

that "[r]esults obtained in animal and in vitro studies *will also be examined*." *Id.* (emphasis added). Ignorant of the existence of the FTC Guidance, Dr. Sano erroneously grounded her entire analysis in her own unsupported, artificially narrow view of what could be considered "competent and reliable scientific evidence." And that led her to restrict her analysis to the Madison Memory Study—and the Madison Memory Study only. She therefore rejected—without considering—the breadth of Quincy's scientific evidence, including open-label studies, animal studies, and *in vitro* studies. In her view, those studies could never be considered "competent and reliable scientific evidence." (*See, e.g.* Dkt. 308-2, Sano Report ¶¶ 28-29; Dkt. 259-10, Sano Tr. at 83:5-9 ("Q. Is it your opinion that an open-label trial does not constitute competent and reliable scientific evidence to support an efficacy claim in a dietary supplement product? A. In general, that's my statement.").) Had Dr. Sano looked at the FTC Guidance, she would have known that that belief too was mistaken. Because she did not consider all of the scientific evidence, however, her analysis departed dramatically from the FTC Guidance's totality-of-the-evidence approach. Plaintiffs cannot rewrite the applicable standard through Dr. Sano's testimony.

Ultimately, Plaintiffs are simply arguing that "competent and reliable scientific evidence" means whatever Drs. Sano and Wittes say it means. That is not the law. Dr. Sano and Dr. Wittes applied their own idiosyncratic standards that mirror the requirements for new drug applications. But Prevagen is not a drug. And their failure to apply the accepted definition of "competent and reliable scientific evidence" in the dietary supplement context means that their opinions are irrelevant. *See, e.g.*, *U.S. v. Wintermute*, 443 F.3d 993, 1001 (8th Cir. 2006) (expert's "proffered testimony misrepresented the government's burden of proving materiality, and by misconstruing the legal question at issue, the testimony was not relevant").

Quincy discussed the court's decision in *Basic Research, LLC v. Federal Trade Commission*, No. 2:09-cv-0779, 2014 WL 12596497 (D. Utah Nov. 25, 2014) in its opening brief. Like Drs. Sano and Wittes, the FTC's expert in that case viewed the proffered scientific substantiation evidence under his own version of the of the "gold standard" of scientific research instead of the definition of "competent and reliable evidence" in the applicable consent order (which mirrored the FTC Guidance word for word). *Id*. at *10-11. That failure, the court explained, meant that the expert's opinion was irrelevant. *Id.* at *11 ("By applying the incorrect standard [the expert's] opinion lack[ed] relevancy because he is opining that Basic Research's evidence does not meet the standard he has put forth, which is not the relevant standard."). Dr. Sano's and Dr. Wittes' opinions suffer from the same foundational flaw and should be excluded.

Plaintiffs relegate *Basic Research* to an afterthought in their Opposition. Indeed, Plaintiffs do not (because they cannot) attempt to meaningfully distinguish it. Instead, Plaintiffs argue only that *Basic Research* is incorrect. (Opp. at 13 n. 5.) But Plaintiffs do not address that court's reasoning or otherwise explain why its result is incorrect. Plaintiffs only cite to—at two separate points in their Opposition—the same line of cases that they have now cited several different times, including in their opposition to Quincy's motion for summary judgment. (Opp. at 7-8, 11; *see also* Dkt. 255 at 10-12.) As discussed extensively in Quincy's summary judgment briefing, those cases involved situations far different from the one here: either the marketing claims in those cases were disease claims or the defendants offered no substantiation evidence whatsoever. (Dkt. 278 at 14-16.) That is not the case here, and Plaintiffs have never argued that it is. In any event, requiring randomized controlled trials ("RCTs") to substantiate disease claims (for example, that a product can "treat, prevent, or reduce the risk of heart disease, prostate cancer, or erectile dysfunction" as was the case in *POM Wonderful, LLC v. Federal Trade Commission*, 777 F.3d 478, 488 (D.C. Cir.

2015), or can cure "cancer, autoimmune diseases, Parkinson's, and heart disease," like in *FTC. v. Direct Mktg. Concepts, Inc.*, 569 F. Supp. 2d 285, 300 (D. Mass. 2008) (cited by Plaintiffs)) is not surprising, as the FTC Guidance specifically requires that marketing claims that make representations about the relationship between a nutrient and a disease be substantiated by "significant scientific agreement." (FTC Guidance at 26 n.2.) That standard is starkly different from the "competent and reliable scientific evidence" standard that applies to structure function claims, which the Challenged Claims undoubtedly are. (*See* Dkt. 222-10, Food and Drug Administration, Small Entity Compliance Guide on Structure/Function Claims (Jan. 2002) ("Examples of acceptable structure/function claims are 'mild memory loss associated with aging,' 'noncystic acne,' or 'mild mood changes, cramps, and edema associated with the menstrual cycle.'"); *see also* Dkt. 225-24, Schwartz Rebuttal Report ¶¶ 15-18.)

But more to the point, none of Plaintiffs' cases discuss the relevance of an expert's opinion that substituted his or her own view of the scientific "gold standard" in place of the FTC Guidance's flexible approach. *Basic Research* did. And the cases that Plaintiffs cite further illustrate how their experts' failure to consider the full range of Quincy's substantiation evidence runs contrary to the FTC Guidance and renders their opinions irrelevant. In *Federal Trade Commission v. Roca Labs, Inc.*, 345 F. Supp. 3d 1375, 1387 (M.D. Fla. 2018), for example, the defendant put forward *no* evidence of substantiation for the marketing claims that it made. Still, the court noted that "the absence of the RCT is just *one piece* of evidence demonstrating the lack of competent and reliable evidence of the truth of the claims or their reasonableness." *Id.* (emphasis added). If the complete absence of a RCT is not dispositive, it follows that Dr. Sano's and Dr. Wittes' critiques of Madison Memory Study (even if they were valid, which they are not) are not dispositive. But that was not the approach that Drs. Sano and Wittes took. They concluded

that the Madison Memory Study alone did not meet their rigid, drug-style standard and, as a result, there was no competent and reliable scientific evidence supporting Quincy's claims. Dr. Sano and Dr. Wittes therefore applied the wrong standard. *See Basic Rsch.*, 2014 WL 12596497, at *10 ("Dr. Blonz, however, only focused on the Andersen/Fogh study rather than looking at the totality of Basic Research's evidence.").

In short, Dr. Sano's and Dr. Wittes' opinions fall far outside of the established framework for assessing whether scientific evidence is "competent and reliable" to substantiate dietary supplement structure function claims. Their testimony is irrelevant because it answers a different question than the one that will be put before the jury. Drs. Sano and Wittes considered whether Quincy's substantiation evidence satisfied their own standard of what counts as "competent and reliable evidence" for drugs, not the standard for dietary supplements found in the FTC Guidance. Their opinions and testimony should therefore be excluded.

B. Drs. Wittes and Sano's "Post Hoc" Assertions Are Unsupported By the Record

Plaintiffs' position throughout this litigation has been that the Madison Memory Study reported statistically significant results from *post hoc* subgroup analyses—which they define as analyses that were conducted after Quincy's researchers reviewed and analyzed the study data. (Compl. ¶ 29.) According to Plaintiffs, "unless researchers document at the outset of a trial all subgroups they intend to use to show efficacy, the researchers would be free to redefine the study population after seeing study data in order to claim findings of significance." (Opp. at 14.)

Despite years of discovery, however, Plaintiffs have failed to uncover any evidence to support their allegation that the analyses reported in the Madison Memory Study (the AD8 0-1 and AD8 0-2 subgroups) were, in fact, *post hoc*, and the undisputed record evidence is to the contrary. But Plaintiffs' experts, like Plaintiffs themselves, simply *assumed* that they were *post hoc.* Both

Dr. Sano and Dr. Wittes admitted that they had no idea when the AD8 0-1 or AD8 0-2 subgroup analyses were planned or when they were conducted. (Mot. at 17-18.) And so, they could not know whether the analyses were *post hoc*. Drs. Sano and Wittes thus offer nothing more than unsupported speculation, which is not reliable expert testimony.

Not only were Drs. Sano's and Wittes' "opinions" about the *post hoc* nature of the subgroup analyses nothing more than assumptions, they are directly contradicted by the record. Drs. Sano and Wittes ignored undisputed testimony from Quincy's President (Mark Underwood) and the principal investigator of the Madison Memory Study (Kenneth Lerner) that the AD8 0-1 and 0-2 subgroup analyses were planned at the outset of the trial. (Dkt. 223, Mark Underwood Declaration in Support of Defendants' Motion for Summary Judgment ¶¶ 25, 28; Dkt. 222-1, Lerner Tr. at 125:19—126:2; Declaration of Glenn T. Graham Ex. O, Underwood Tr. at 92:21—93:8, 94:15—95:9.)[2] That testimony is further corroborated by the number of participants in the Madison Memory Study. The study protocol indicated a sample size of 100 participants, and there were exactly 100 participants who scored between a 0 and 2 on the AD8 scale. (Dkt. 223-16, QUI-FTCNY-00068424-00068429 at 00068425; Dkt. 223-17, QUI-FTCNY-00003696-3705 at 00003700.) As Quincy's expert Dr. Wei testified, there would be a "very small chance" of the protocol matching the actual number of participants in the AD8 0-2 group purely by chance. (Graham Reply Decl. Ex. P, Wei Tr. at 146:13—148:21, 226:2-17.) Drs. Sano and Wittes either ignored or were not shown this evidence. (Dkt. 259-10, Sano Tr. at 126:9-17, 127:7-14; Dkt. 259-11, Wittes Tr. 102:21—104:4; *see generally* Dkt. 308-6, Wittes Report Exhibit B.)

[2] All references to "Ex." are to the exhibits to the Declaration of Glenn T. Graham dated October 21, 2022 and filed herewith in further support of Quincy's Motion to Exclude Plaintiffs' Experts ("Graham Reply Decl.").

Accordingly, Drs. Sano and Wittes' assumptions that the AD8 0-1 and AD8 0-2 analyses were "*post hoc*" are contrary to the record, wildly speculative and do not "fit" Plaintiffs' case. Such unreliable testimony should be excluded.[3]

Instead of addressing the evidence that refutes their experts' assumptions, Plaintiffs attempt to redefine what it means for an analysis to be *post hoc*. They argue that "Drs. Sano and Wittes, applying the standards of their fields, opined that analyses of subgroups not pre-specified in the study protocol are, *by definition*, *post hoc* in nature and are inherently unreliable." (Opp. at 14 (emphasis in original).) That definition— is inconsistent with the prevailing view of experts in clinical trial design and analysis. And Drs. Sano and Wittes testified as much, undermining Plaintiffs' argument on this point in the process.

At their depositions, Drs. Sano and Wittes both agreed with a definition of "*post hoc*" analysis that does *not* require pre-specification in a study protocol. (Dkt. 259-10, Sano Tr. at 195:3—197:8; Dkt. 259-11, Wittes Tr. at 88:19—91:17.) According to an article published in the New England Journal of Medicine, "[a] prespecified subgroup analysis is one that is planned and documented *before any examination of the data*, preferably in the study protocol." (Graham Reply Decl. Ex. Q, QUI-FTNY-00187075-00187080 (emphasis added).) Under this agreed-upon definition, pre-specification of a subgroup analysis is not required to be stated in a study's protocol so long as the analysis is decided upon prior to the examination of the study's data. (Dkt. 259-10, Sano Tr. at 195:3—197:8; Dkt. 259-11, Wittes Tr. at 88:19—91:17.) It follows that although

[3] Plaintiffs accuse Defendants of citing to a "partial" answer from Dr. Sano's deposition demonstrating that she "assumed" that the subgroup analyses were decided upon and conducted after the "overall" analysis. (Opp. at 13.) While Defendants dispute that characterization, they hereby attach a longer excerpt from Dr. Sano's deposition, which further confirms Dr. Sano's speculation. (*See* Dkt. 259-10, Sano Tr. at 184:2—189:12.) Critically, Dr. Sano testified that the document she relied upon for her "*post hoc*" conclusion did not "give any suggestion of when these alleged subgroup analyses were performed," that she did not "know when any of these alleged subgroup analyses were performed," that she had not seen "any documents that give any information about when any alleged subgroup analysis was conducted," and that she "assume[d] that they did the overall first and the secondaries after." (*Id.*)

inclusion in a protocol is one way of showing pre-specification, it is not the only way. And under that definition, Mr. Underwood and Mr. Lerner's undisputed testimony that the AD8 0-1 and AD8 0-2 subgroups were planned—upends Drs. Sano and Wittes' unsupported opinions that the subgroup analyses were *post hoc*.

In an attempt to distract from their experts' critical admissions made at their depositions, Plaintiffs now point to what they characterize as "a wide range of evidence to support [Drs. Sano's and Wittes'] opinion that the AD8 0-1 and 0-2 subgroups were not the study's target population." (Opp. at 14.) Plaintiffs cannot sidestep Dr Sano's and Wittes' own admissions that their opinions were based on speculation and assumptions and attempt to rehabilitate their experts' opinions through attorney argument. *See Almeciga v. Ctr. for Investigative Reporting, Inc.*, 185 F. Supp. 3d 401, 426 (S.D.N.Y. 2016) (finding that the "number of striking contradictions between [the expert's] Report and her in-court testimony" renders her opinion "fundamentally unreliable and critically flawed"); *Chartier v. Brabender Technologie, Inc.*, No. 4:08-cv-40237,, 2011 WL 4732940, at *8 (D. Mass. Oct. 5, 2011) (excluding statements in an expert report "that were directly contradicted by [the expert's] later deposition testimony[] and as to which no satisfactory explanation [for the contradiction] has been given"). That said, none of this evidence has anything to do with *when* the AD8 0-1 and 0-2 subgroup analyses were planned and, in some instances, the cited evidence actually contradicts Plaintiffs' arguments.

For example, Plaintiffs point to "multiple study write-ups and the deposition testimony of Kenneth Lerner, all of which referenced a study population of over 200 subjects, over twice the number of subjects in the two subgroups." (Opp. at 15.) But the total number of study participants is not probative of when Quincy decided to analyze the AD8 0-1 and 0-2 subgroups, especially given that (1) Mr. Underwood and Mr. Lerner both offered undisputed testimony that Quincy

decided to analyze the Madison Memory Study data by AD8 scores at the outset of the trial, and (2) the sample size in the protocol exactly matched the number of participants in the AD8 0-2 population.

Plaintiffs likewise argue that the inclusion and exclusion criteria in the protocol are not *expressly* correlated to the AD8 screening tool. (Opp. at 15.) Plaintiffs do not take issue with Quincy's *use* of the AD8 screening tool; instead their concern is that it was not expressly mentioned in the protocol. More specifically, Dr. Sano appears to question whether the AD8 was used at all during the study, as opposed to just being reported after the fact as part of Quincy's so-called "*post hoc*" analyses. (Dkt. 259-10, Sano Tr. at 124:18—126:8.) Dr. Sano's concern is undermined by the protocol itself, which references a screening phase, as well as Mr. Lerner's undisputed testimony that the AD8 "was part of the original study." (Graham Reply Decl. Ex. R, Lerner Tr. at 63:25—64:16.)[4]

Plaintiffs also assert that "Defendants did not randomize study subjects by AD8 score, or group of scores." (Opp. at 15.) Again, randomization by AD8 score simply is not probative of whether Quincy intended to analyze the AD8 0-1 and 0-2 subgroups from the outset of the study. But more importantly, the randomization ratio used for the Madison Memory Study was 2:3; in other words, for every two participants who were assigned to the placebo arm of the study, three participants were assigned to the apoaequorin arm. (Dkt. 223-17, QUI-FTCNY-00003696—QUI-FTCNY-00003705 at 00003697.) Notably, this 2:3 randomization ratio was maintained for the target population of the study (AD8 0-2) even if not for the other AD8 scores. Of the 100 participants in the AD8 0-2 group, 40 were assigned to the placebo arm of the study and 60 were

[4] Dr. Sano must have either ignored or overlooked these portions of Mr. Lerner's deposition testimony, which she claims to have reviewed in connection with her affirmative report. (Dkt. 308-2, Sano Report Attachment B at 3.)

assigned to the apoaequorin arm of the study —a ratio of 2:3. (*Id.* at 00003700.) Neither Dr. Sano nor Dr. Wittes addressed this evidence, which further refutes their unfounded assumptions that the AD8 0-2 group was not the population of interest from the outset of the study.

Next, Plaintiffs point to a "list of subgroups" that include subgroups of participants other than those scoring from 0 to 2. (Opp. at 15.) However, the fact that Quincy may have[5] conducted additional exploratory subgroup analyses does not mean that the 0-1 and 0-2 groups were not planned before researchers reviewed the data or otherwise suggest that the 0-1 and 0-2 analyses were *post hoc*. When presented with this "list" of subgroup analyses at her deposition, Dr. Sano testified that "[t]he assumption [she] made was that all of them were exploratory, with the exception of the initial analyses" of the "entire study population." (Dkt. 259-10, Sano Tr. at 204:18—205:25.) Presumably because that is what Plaintiffs told Dr. Sano to assume despite having record evidence to the contrary of such an assumption. Dr. Sano's assumption was based on nothing more than the "order" the subgroups were listed on the document, which was dated more than five years after the study's completion, and Dr. Sano eventually conceded that she did not know whether *any* of the subgroups listed—*including* the AD8 0-1 and AD8 0-2—were exploratory or not. (Dkt. 259-10, Sano Tr. at 210:8-13.)

Plaintiffs also cite two of "Defendants' interim press releases regarding the Madison Memory Study results, none of which referenced subgroups." (Opp. at 15.) These press releases (one of which appears to be a draft (QUI-FTC-0015870)) say nothing about when Quincy decided to analyze the AD8 0-1 and 0-2 subgroups and, at most, suggest that Quincy *also* intended to analyze the entire data set, which is not in dispute.

[5] Dr. Sano testified that she did not even know whether each of the subgroup analyses listed in this document were actually conducted. (Dkt. 259-10, Sano Tr. at 210:16-20.)

Finally, references to the AD8 2-5 subgroup in certain publications does nothing to change the fact that the Madison Memory Study's target population was healthy, older adults—i.e., those in the 0-1 and 0-2 groups. Indeed, for example, the peer-reviewed journal write up of a subset of the Madison Memory Study's results (*Effects of a Supplement Containing Apoaequorin on Verbal Learning in older Adults in the Community*) merely reported *additional* positive data with respect to individuals scoring between 2-5. (Dkt. 223-20, QUI-FTCNY-00003815—QUI-FTCNY-00003816.) None of this supports the speculative assertions made by Plaintiffs' experts about when the target population was identified.

For all of these reasons, the testimony of Drs. Sano and Wittes relating to the so-called "*post hoc*" subgroup analyses are unsupported, unreliable, unduly speculative, and should be excluded. *See Buckley v. Deloitte & Touche USA LLP*, 541 F. App'x 62, 64 (2d Cir. 2013); *ECD Inv. Grp. v. Credit Suisse Int'l,* No. 14-cv-8486, 2017 WL 3841872, at *14 (S.D.N.Y. Sept. 1, 2017); *Munn v. Hotchkiss Sch.*, 24 F. Supp. 3d 155, 203 (D. Conn. 2014); *Macaluso v. Herman Miller, Inc.*, No. 7:01-cv-11496, 2005 WL 563169, at *8 (S.D.N.Y. Mar. 10, 2005).

II. DR. BERG'S TESTIMONY REMAINS UNRELIABLE AND IRRELEVANT AND SHOULD BE EXCLUDED

A. Plaintiffs Fail to Acknowledge that Dr. Berg Lacks the Qualifications Necessary to Render His Conclusions

Plaintiffs' argument that "Dr. Berg does not need to be an expert on memory or cognition" or on human digestion in order to opine on whether Prevagen "could produce any effect on *memory or cognition*" (Dkt. 308-9, Berg Report ¶ 7 (emphasis added)), defies logic. In fact, Dr. Berg ultimately concludes that there is no evidence that Prevagen has any therapeutic effect *at all* (including, but not limited to, on memory or cognition.) (*Id.* ¶¶ 14, 51.) (This despite the fact that he offered no conclusions at all about the numerous trials and studies that demonstrated an actual therapeutic effect.) Dr. Berg's opinions about memory and cognition therefore form the basis for

his ultimate conclusions (*see generally id.*, Berg Report ¶¶ 24-30). At the same time, however, Dr. Berg *admitted* that he is not an expert in either memory or cognition (Dkt. 308-11, Berg Tr. at 35:11-16) or in human digestion (*id* at 53:7-11), making him patently unqualified to render these conclusions.

Plaintiffs' arguments to the contrary ignore the breadth and infirmity of Dr. Berg's conclusions. In their Opposition, Plaintiffs argue that Dr. Berg is qualified to opine "on the characteristics of apoaequorin, and why those characteristics make it *unlikely* that apoaequorin – a protein that is digested like other dietary proteins – could have any effect on the human body." (Opp. at 35.) But that is a complete whitewash of Dr. Berg's opinion. Dr. Berg does not limit his conclusion to why apoaequorin's characteristics make it *unlikely* that apoaequorin has an impact on the human body (including on memory or cognition). Instead, Dr. Berg concludes with the much broader proposition that he "ha[s] not seen evidence in the literature or otherwise that apoaequorin could have *any* effect on the human body through *any other* mechanism of action" whatsoever. (Dkt. 308-9, Berg Report ¶ 55.) And he goes even one step further in his pretrial declaration, asserting that "it is *clear* that Prevagen and its active ingredient apoaequorin have not been shown to have *any* therapeutic effect on humans." (Dkt. 297, Berg Pretrial Declaration ¶ 15 (emphasis added).) To make such a broad conclusion—that the way apoaequorin is digested by the human body means it can have *no therapeutic effect*—Dr. Berg does, in fact, need to be an expert in human digestion, and perhaps in other areas of science as well. Thus, while Plaintiffs may be correct that Dr. Berg is an expert in "biochemistry, physiology, pharmacology," Dr. Berg is *not* an expert in fields that are critical to the expansive conclusions he attempts to draw.

B. Plaintiffs' Arguments Regarding the Reliability of Dr. Berg's Conclusions Fail to Acknowledge Their Breadth

Furthermore, Plaintiffs' defense of Dr. Berg's conclusions regarding Prevagen's

mechanism of action ignores that Dr. Berg fails to provide sufficient support for his conclusion that Prevagen lacks a *plausible* mechanism of action. (Dkt. 308-9, Berg Report ¶¶ 51-55.) For such an overbroad conclusion to be credible—i.e., to exclude the possibility of *any* plausible mechanism of action—Dr. Berg would have had to venture far beyond Defendants' evidence regarding apoaequorin's biological characteristics and therapeutic effect and assess all other *possible* mechanisms of action to determine which, if any, were plausible. But Dr. Berg did not do this, nor is he qualified to do so. Indeed, Dr. Berg admitted at deposition that at least one of the potential mechanisms of action for Prevagen—the gut-brain access—*remains viable*, directly contradicting his conclusions. (Dkt. 308-11, Berg. Tr. at 88:2—89:7.) This "fundamental" inconsistency between Dr. Berg's report and his deposition testimony further undercuts its admissibility, since Rule 26 requires that "expert witnesses [] generally be held to their testimonial concessions, particularly where those concessions contradict their earlier expert reports." *Chartier*, 2011 WL 4732940, at *8; *see also Almeciga*, 185 F. Supp. 3d at 426. Dr. Berg failed to even consider other mechanisms, including those identified by Defendants' expert Dr. Gortler, leaving his opinions unreliable at best.[6] Those opinions should be excluded from trial.

Recognizing the deficiencies in Dr. Berg's testimony, Plaintiffs argue in the alternative that the significant issues with Dr. Berg's report provide fodder for cross-examination but do not warrant exclusion. Plaintiffs are wrong. Courts in this Circuit have excluded expert testimony where the "expert lacks good grounds for his or her conclusions." *Amorgianos v. Nat'l R.R. Passenger Corp.*, 303 F.3d 256, 267 (2d Cir. 2002); *see also In re LIBOR-Based Fin. Instruments*

[6] Plaintiffs' arguments that Dr. Berg "cannot be faulted" for failing to consider the theories offered by Dr. Gortler regarding Prevagen's potential mechanisms of action further underscore the unreliability of Dr. Berg's report. Dr. Berg concluded in his report that there is *no plausible* mechanism of action for Prevagen (Berg Report ¶ 55), and Dr. Gortler quickly and credibly refuted by way of rebuttal that conclusion by presenting a number of plausible mechanisms of action for Prevagen that Dr. Berg simply did not consider. That Dr. Berg was not "on notice" of these potential mechanisms of action is irrelevant to the existence of these other potential mechanisms of action.

Antitrust Litig., 299 F. Supp. 3d 430, 468 (S.D.N.Y. 2018) (calling for exclusion of expert testimony "when an expert opinion is based on data, a methodology, or studies that are simply inadequate to support the conclusions reached"). And this Court's opinion in *In re Fosamax Products Liability Litigation*, 645 F. Supp. 2d 164 (S.D.N.Y. 2009), cited by Plaintiffs, is readily distinguishable. There, the Court concluded that an epidemiologist who had conducted significant research on osteoporosis and osteoporosis treatments was qualified to interpret and offer opinions on epidemiological evidence on osteoporosis despite certain deficiencies in her report. *Id.* at 207-08. But that is far from the case here; Dr. Berg *lacks any* expertise on memory, cognition, or human digestion (despite rendering the conclusion that Prevagen has no therapeutic effect on memory or cognition based on how it is digested by the human body). And, despite this, he offers sweeping conclusions regarding Prevagen's *plausible* mechanisms of action and therapeutic effect that completely lack factual or scientific support. Indeed, while Plaintiffs argue that Dr. Berg has presented "reasonable explanations" for his overbroad, unsupported conclusions, Dr. Berg has failed to provide *any* explanations for his admitted failure to consider other, plausible mechanisms of action for Prevagen. (Dkt. 308-11, Berg Tr. at 88:2—89:7.) He has also admittedly failed to acknowledge that a number of other drugs and substances available on the market—aspirin, acetaminophen, ibuprofen, and an entire class of antidepressants—were deemed clinically effective *long before* (and independent of) the ultimate identification of their respective mechanisms of action. (*Id.* at 86:22—87:15.) Dr. Berg's material oversights are precisely the type that courts have cited as a basis for excluding expert testimony.

C. Plaintiffs' Arguments Regarding the Gut-Brain Axis as a Potential Mechanism of Action for Apoaequorin Similarly Ignore the Breadth of Dr. Berg's Conclusions

Plaintiffs spend significant ink attempting to refute Defendants' argument that the "gut-brain axis" remains a *plausible* mechanism of action for Prevagen and therefore undermines Dr.

Berg's conclusions to the contrary. But despite Plaintiffs' attempt to change the narrative, they cannot avoid Dr. Berg's admissions: that the gut-brain axis is a topic of "much current interest" (Dkt. 259-13, Berg Rebuttal Report ¶ 30) and that the gut-brain axis is the subject of many articles in one of the publications where he served as editor-in-chief (Dkt. 308-11, Berg Tr. at 76:8—85:7)—and that Dr. Berg, as editor-in-chief, would not have allowed the publication of an implausible theory.[7] (*Id.* at 77:8-10.) Finally, while Dr. Berg summarily concluded *in his report* that the gut-brain axis was an "implausible and unsupported mechanism" for Prevagen (Berg Report ¶ 50), he admitted *at his deposition* that he did not recall "rel[ying] on anything specifically" to draw this summary conclusion. (Berg Tr. at 84:16-21.) It is telling that, in arguing that Dr. Berg has expertise to opine on the gut-brain axis, Plaintiffs rely on a couple of "seminars" Dr. Berg once took and another course he "probably" took at some other time—these are hardly suggestive of any actual expertise. (Opp. at 42.) Indeed, Dr. Berg himself testified at his deposition that he has not done any studies on the gut-brain axis and that it is not part of his primary area of research. (Dkt. 308-11, Berg Tr. at 72:13-18.) Ultimately, no amount of hand-waving can change the fact that Dr. Berg stepped well-outside his areas of expertise and drew an overbroad conclusion about Prevagen's *plausible* mechanisms of action and its relationship with Prevagen's therapeutic effectiveness that Dr. Berg does not—and cannot—support.

D. Dr. Berg's Testimony Regarding Prevagen's Mechanisms of Action is Not Relevant in Assessing its Therapeutic Effect

Plaintiffs' efforts to demonstrate the relevance of Dr. Berg's testimony shows precisely why it should be excluded. It is quite simple: Dr. Berg concludes in his report that because he is incapable of pointing to a mechanism of action for Prevagen, it cannot have any therapeutic effect

[7] It is ironic that Plaintiffs dismiss the fact that these articles about the plausibility of the gut-brain axis in *Science* were published under Dr. Berg's tenure as editor-in-chief (Opp. at 41), but then attempt to rely on the fact that those articles were published as some sort of evidence that Dr. Berg has expertise in this area of study. (Opp. at 42.)

on the human body. (Berg Report ¶¶ 51, 55.) By the same logic, most pain relievers would not have been available until recent years, and headaches, fevers and, treatable pain would have remained untreatable. (Dkt. 305-8, Gortler Report ¶¶ 36-37; Dkt. 225-22, Schwartz Rebuttal Report ¶¶ 27-28; Dkt. 308-11, Berg Tr. at 86:22—87:10.) And Plaintiffs are aware that this cannot be the case, conceding that a "'definitively known' or 'fully elucidated' mechanism of action is not required for clinical efficacy of dietary supplement." (Opp. at 43.) Thus, despite Plaintiffs' attempt to spin Dr. Berg's report, this concession alone negates the broad conclusions made by Dr. Berg in his report, and renders his testimony irrelevant.

III. PLAINTIFFS SHOULD BE PRECLUDED FROM INTRODUCING ANY TESTIMONY FROM DR. MALASPINA AT TRIAL

A. Dr. Malaspina is Not Qualified to Render the Opinions He Offers About SAS Computer Programming and the Proper Interpretation of Clinical Trial Data

Plaintiffs argue that Dr. Malaspina is qualified to offer his opinions because he is an expert in "economics, econometrics, and statistics generally, and with the SUR model specifically." (Opp. at 20.) But this is a misdirection. Dr. Malaspina's opinion is not one of economics, econometrics, or statistics—rather, it is an opinion about the proper way to program a SUR analysis in the SAS programming language. On that issue, Dr. Malaspina has no experience—or at least no experience he can remember.

Plaintiffs admit that Dr. Malaspina's task was to determine whether Dr. Beales "properly programmed" his model. (Opp. at 20.) To do so, Dr. Malaspina "reviewed the code programmed by Dr. Beales and the associated output" and concluded from a "facial analysis of the code and its associated output" that the model was supposedly programmed incorrectly. (*Id.* at 19.) Next, Dr. Malaspina purported to "correct Dr. Beales' fundamental programming errors—by keeping Dr. Beales' model specification but changing his code" in various ways. (*Id.*) Based on this review of the programming code, Dr. Malaspina purports to opine that "by erroneously programming his

model," Dr. Beales failed to perform the SUR analysis he claimed to be performing. (*Id.* at 18.) It is therefore obvious that Dr. Malaspina's opinion is chiefly about computer programming, not economics, econometrics or statistics.

Dr. Malaspina is not, and does not claim to be, an expert in the use of the PROC MIXED statement in the SAS computer language. As the SAS user manual makes clear, the PROC MIXED statement is a complex computer function with many optional commands that can be added to modify its functionality and achieve different results. (*See generally* Dkt. 314-4, 314-5.) Someone purporting to testify that Dr. Beales "erroneously programmed" his model by misusing the PROC MIXED statement should, at a minimum, have some experience with that function of the SAS programming language. *See Barban v. Rheem Textile Sys., Inc.*, No. 01-cv-8475 (ILG), 2005 WL 387660, at *4 (E.D.N.Y. Feb. 11, 2005), *aff'd*, 147 F. App'x 222 (2d Cir. 2005); *523 IP LLC v. CureMD.Com*, 48 F. Supp. 3d 600, 645-46 (S.D.N.Y. 2014). Dr. Malaspina, however, has no such experience that he could recall at his deposition or that he could muster in opposition to this Motion. Instead, Plaintiffs merely argue that "it's possible" Dr. Malaspina used the PROC MIXED function before this litigation. (Opp. at 23.)

In fact, at his deposition, Dr. Malaspina repeatedly professed ignorance about key portions of the SAS user manual concerning how to program mixed models like an SUR. For example, when confronted with a portion of the manual that contradicted one of his main opinions about how Dr. Beales supposedly programmed his model incorrectly, Dr. Malaspina admitted that he was "just looking at [this portion of the manual] for the first time." (Dkt. 308-13, Malaspina Tr. at 72:22—73:15.) When questioned further, Dr. Malaspina stated "I'm trying to figure out what they're getting at. And I don't think I can really just sit here and figure it out on the fly." (*Id.* 74:24—75:4.) Similarly, Dr. Malaspina also criticized Dr. Beales for using a particular option in

his program that dictated how a certain matrix was constructed (TYPE=VC), but admitted that he had only read about the various matrix options offered in the SAS programming language in connection with his work on this litigation. (*Id.* 82:15—83:15.) Plaintiffs' argument that the SAS user guide is long and that experts often refer to the guide while programming their models (Opp. at 23) is no defense to Dr. Malaspina's lack of expertise in using the applicable functions. The case law is clear that an expert cannot opine on areas that he only learns about while preparing his opinion for the litigation. *See In re Mirena IUD Prod. Liab. Litig.*, 169 F. Supp. 3d 396, 439 (S.D.N.Y. 2016).

Finally, Dr. Malaspina admittedly has never actually performed any clinical analyses like the one he purports to rebut here. (Dkt. 308-13, Malaspina Tr. at 24:7—25:7; 27:14-20; 32:3-9; 34:10-17.) That too renders him unqualified. In opposition, Plaintiffs argue that Dr. Malaspina's opinion does not really concern clinical trials. (Opp. at 20-21.) But Dr. Malaspina recognized in his report that "[a]t the center of the relevant issues in this report is data from the Madison Memory Study." (Dkt. 308-12, Malaspina Report ¶ 19.) Indeed, the population of data for Dr. Malaspina's analysis were the MMS study participants, and the data points for the analyses comprised of the CogState test results over time. (*Id.* ¶¶ 20-21.) In fact, Dr. Malaspina's purported "correction" to Dr. Beales' model itself concerned the "correlation across the nine different CogState Test Types and across individuals repeated test results over time" because Dr. Malaspina concluded that Dr. Beales' analysis "effectively treat[ed] each individual's five days of test results as it would a single day of test results from five individuals." (*Id.* ¶¶ 39-42.) Thus, in order to rebut an analysis of this type of data an expert should have relevant experience interpreting clinical trial data. Dr. Malaspina does not.

B. Dr. Malaspina's Opinions Regarding the SUR Analysis Are Not Reliable and Will Not Assist the Trier of Fact

a. Dr. Malaspina Conceded that the "Corrected" Analysis Underlying His Opinions Regarding the SUR Is Not Reliable

Dr. Malaspina's so-called "correction" of Dr. Beales' analysis is unreliable and Plaintiffs' repeated attempts to draw conclusions from those "corrections" should be rejected. As Plaintiffs acknowledge, Dr. Malaspina's report explicitly stated that he does "not opin[e] that his corrections are sufficient to fully recover Dr. Beales' analysis such that [it] is suitable to draw reliable conclusions about the available data." (Dkt. 308-12, Malaspina Report ¶ 14 n.15; Dkt. 308-13, Malaspina Tr. at 154:10.) Plaintiffs attempt to limit this admission by arguing that Dr. Malaspina's statement is being misconstrued and taken out of context, positing that Dr. Malaspina was actually referring to "whether his correction to Dr. Beales's analysis makes *Dr. Beales's analysis* suitable for drawing reliable conclusions." (Opp. at 25 (emphasis added).) But Plaintiffs' interpretation of Dr. Malaspina's statement is contradicted by his own deposition testimony. Dr. Malaspina unmistakably explained that what he meant by his footnote was that *his* "modified analysis"—not Dr. Beales' analysis—is not suitable to draw reliable conclusions. (Dkt. 308-13, Malaspina Tr. at 154:13-18.)

Even worse, Dr. Malaspina's Report is rife with conclusions premised on the end results of the same "modified analysis" that he concedes is unreliable.[8] For example, Dr. Malaspina asserts that after implementing his "corrections" to Dr. Beales' analysis, "*[t]hese corrections show* that under Dr. Beales' own test criteria" there is no statistical significance and "thus *prov[e]* that Dr. Beales's analysis is unreliable." (Dkt. 308-12, Malaspina Report ¶ 7 (emphases added).) In

[8] In addition to Dr. Malaspina, Plaintiffs also erroneously drew conclusions based on the outputs of Dr. Malaspina's "correction" to Dr. Beales' model while attempting to exclude Dr. Katz, arguing that Dr. Katz "fail[ed] to realize" the "results" attained from Dr. Malaspina's "corrected" model. (Dkt. 304 at 16-17.)

doing so, Dr. Malaspina explicitly relies on the "corrected" analysis in reaching his conclusion despite its admitted unreliability. In fact, Dr. Malaspina restates his overarching conclusion that implementing "these corrections show" that "there is no evidence that Prevagen has a statistically significant effect" on three separate occasions in his report. (*Id.* ¶¶ 7, 14, 39.) Dr. Malaspina also testified that his conclusion that there is no statistical significance in the MMS is "based on [his] partial correction to Dr. Beales." (Graham Reply Decl. Ex. T, Malaspina Tr. at 110:17-23.) If permitted to testify at trial, Dr. Malaspina will similarly testify that "when you correct Dr. Beales's re-analysis to comply with the assumptions of a SUR model, *the results* are not statistically significant." (Opp. at 17 (emphasis added).)

Dr. Malaspina cannot have it both ways. He cannot admit that his corrections are not suitable for drawing conclusions and then, at the same time, rely on those corrections to attack Dr. Beales' analysis and, by extension, a portion of Dr. Katz's opinion. Dr. Malaspina's conclusions based on his "modified analysis" are, by his own admission, unreliable. Those opinions should therefore be excluded.

b. Dr. Malaspina's Admitted Reliance on a Technique that Was Not Called for in the Analysis He Purports to "Correct" Will Not Assist the Trier of Fact.

Dr. Malaspina's opinions about his supposed "correction" to Dr. Beales' model are also irrelevant because he admittedly utilized an entirely new model from the one he is purportedly "corrected." Dr. Malaspina claimed that he was able to demonstrate that Dr. Beales' original model was flawed by "keeping Dr. Beales' model specification[] but changing his program to allow for the correlation that was purportedly accounted for." (Dkt. 308-12, Malaspina Report ¶ 39.) But Dr. Malaspina conceded at his deposition—and Plaintiffs did not address—that he was *not* able to keep Dr. Beales' original model as claimed and that his attempts to do so "didn't work." (Dkt. 308-13, Malaspina Tr. at 144:23—145:6.)

In order to account for the random effects contemplated in Dr. Beales' report, Dr. Malaspina attempted to implement an unstructured variance matrix, which "seemed to [Dr. Malaspina] something that would approximate the freedom that a . . . mixed model with SUR analysis with random effects would." (Dkt. 308-13, Malaspina Tr. at 88:25—89:11.) Thus, incorporating the unstructured variable would allow Dr. Malaspina to keep the original model and change it to resemble "Dr. Beales's stated description." (Opp. at 28.) But Dr. Malaspina's attempts to "keep Dr. Beales's model specification" while implementing the desired random effects failed; the program got "hung up" and "couldn't find a solution" at all.[9] (Dkt. 308-13, Malaspina Tr. at 90:10—91:21.) The fact that Dr. Malaspina could not successfully complete the corrected analysis he claims to perform makes his entire opinion unreliable and unhelpful to the trier of fact.

Plaintiffs claim that Dr. Malaspina's application of the bootstrap method is relevant because it "explains the flaws in Dr. Beales's analysis." (Opp. at 28.) But this ignores the fact that the bootstrap method is not a "correction" to Dr. Beales' program—it is an entirely new method of analysis, programmed in a different computer language (STATA). The bootstrap method works by "sampling with replacement" and then "running the model on a subset based on that sample, and doing it again" and again to "see[] how [its] results change in the variance of those results." (Graham Reply Decl. Ex. T, Malaspina Tr. at 105:24—106:8.) This does not

[9] While Plaintiffs argue that omitting mention of this analysis from Dr. Malaspina's report was not "cherry picking" because he "did not, and could not, consider output that simply does not exist," (Opp. at 26), Dr. Malaspina admitted that the reason he did not include it was because he did not believe it to be "necessary to reach the conclusions [he] was making." (Dkt. 308-13, Malaspina Tr. at 90:5-9.) Given Dr. Malaspina's initial attempt to implement an unstructured variable because it approximated the random effects purportedly missing from Dr. Beales' analysis, the methods tested by Dr. Malaspina while developing his "correction" bear directly on the Court's analysis as to its reliability. *See Schwab v. Philip Morris USA, Inc.,* No. 04-cv-1945, 2006 WL 721368, at *3 (E.D.N.Y. Mar. 20, 2006) ("Adverse material reviewed and rejected by an expert bears on his credibility, the soundness of his techniques, and the weight to be given his conclusions. It may be relevant to the court's decision whether to qualify under *Daubert.*").

resemble Dr. Beales' model—it is an entirely new and independent analysis masquerading as a "correction." As such, allowing Dr. Malaspina to testify about this purportedly "corrected" data will not help the trier of fact ascertain the accuracy of Dr. Beales' original analysis. Rather, Dr. Malaspina's testimony concerning his new SUR model instead will mislead the jury about the analyses at issue and runs a higher risk of confusing the jury about analyses not before it. *See Washington v. Kellwood Co.*, 105 F. Supp. 3d 293, 307-08 (S.D.N.Y. 2015).

C. Dr. Malaspina's Opinions Regarding the Bonferroni Correction Are Unreliable and Irrelevant

Plaintiffs claim that Dr. Malaspina's opinions concerning the Bonferroni correction are admissible because Dr. Katz supposedly suggested that a SUR analysis and the Bonferroni correction are "mutually exclusive." (Opp. at 28-29.) But nowhere in his report did Dr. Katz ever opine that applying the Bonferroni correction is "mutually exclusive" with a SUR analysis; rather, Dr. Katz stated that "the Bonferroni correction is not appropriate *here*." (Dkt. 220-15, Katz Report ¶ 57 (emphasis added).) Dr. Katz explained that "[t]he proper use of Bonferroni is to avoid the elevated risk of false positives with multiple, independent hypothesis testing" and that it was not needed here because "there is no evidence of multiple hypothesis testing" in the MMS. (*Id.*)

Dr. Malaspina purports to opine only that a Bonferroni correction is compatible with a SUR analysis but, as Plaintiffs admit, there is no disagreement between Drs. Malaspina and Katz on this irrelevant point. (Opp. at 29.) Dr. Katz's opinion concerns the application of the Bonferroni correction to the specific facts of the Madison Memory Study. Plaintiffs do not even attempt to explain how Dr. Malaspina's statement that a SUR "is perfectly compatible with the Bonferroni correction" rebuts Dr. Katz's fact-specific conclusion about its applicability in this particular instance. Moreover, Dr. Malaspina admitted that the Bonferroni correction "may or may not be appropriate depending on the specific facts of what you're looking at" and admitted *three separate*

times that he is not opining on whether the Bonferroni correction would be appropriate for use on the Madison Memory Study data. (Dkt. 308-13, Malaspina Tr. at 155:25—156:5; 170:3—171:1.)[10] As such, Dr. Malaspina's concession that his rebuttal opinion does not address Dr. Katz's actual conclusion necessarily renders his opinion "not relevant and, *ergo*, non-helpful." *In re Elysium Health-ChromaDex Litig.*, No. 17-cv-7394, 2022 WL 421135, at *30 (S.D.N.Y. Feb. 11, 2022) (quoting *Daubert v. Merrell Dow Pharms., Inc.*, 509 U.S. 579, 591, (1993)).

CONCLUSION

For the foregoing reasons, and for the reasons set forth in their moving brief, Defendants respectfully request that this Court grant their Motion to Exclude Plaintiffs' Experts in its entirety, along with such other and further relief as the Court deems appropriate.

[10] Nor would Dr. Malaspina be qualified to opine on the appropriateness of the Bonferroni correction, as he admittedly has no experience in analyzing clinical trial data. (Dkt. 308-13, Malaspina Tr. at 20:14-23; 27:4-24; Opp. at 17, 20 (noting Dr. Malaspina's purported expertise in economics, econometrics and statistics).)

Date: October 21, 2022

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CERTIFICATE OF SERVICE

I certify that on this 21st day of October, 2022, I caused to be served Defendant's Reply Memorandum of Law in Further Support of Defendants' Motion to Exclude Plaintiffs' Experts, to be made by electronic filing with the Clerk of the Court using the CM/ECF system, which will send a Notice of Electronic Filing to all counsel of record.

Date: October 21, 2022

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